Remarks

Claims 1, 3-5, 11-13, 22, 23, 25, and 38-43 are currently pending. Claim 2 has been canceled. Claim 1 has been amended to include the limitations of claim 2, and claims 3 and 4 have been written in independent form. Claim 5 has been amended to remove the "molecules having sequence similarity to TGF-ß" limitation. Claims 22 and 25 have been amended to include the "wherein said fragment increases the degree or rate of osteogenesis or calcification by BMP-2" limitation.

Claims 1, 22, 25, and 43 stand rejected under 35 U.S.C. §112 first paragraph. Claim 5 stands rejected under 35 U.S.C. §112, second paragraph. Claims 1-4, 12, 13, 22, 25, and 38-40 stand rejected under 102(b). Applicants respectfully traverse the rejections.

Rejections Under 35 U.S.C. §112

The Examiner rejected claims 1, 22, 25, and 43 under 35 U.S.C. §112, first paragraph, for failing to comply with the enablement requirement. Specifically, the Examiner argued that the specification "does not reasonably provide enablement for a peptide comprising a fragment of SEQ ID No: 1 without regard to the structure or function of the fragment." However, the Examiner acknowledges that the specification is enabling for "a fragment of SEQ ID NO: 1, wherein said fragment increases the degree or rate of osteogenesis by BMP-2." Claims 1, 22, and 25 have been amended to include "wherein said fragment increases the degree or rate of osteogenesis by BMP-2." Claim 43 is dependent on claim 25, which now includes "wherein said fragment increases the degree or rate of osteogenesis by BMP-2." Thus, Applicants respectfully submit that claims 1, 22, 25, and 43 are enabled under 35 U.S.C. §112, first paragraph.

The Examiner rejected claim 5 under 35 U.S.C. §112, second paragraph, for indefiniteness. Specifically, the Examiner argued that "Claim 5 is indefinite over the recitation of 'molecules having sequence similarity to TGF ß.'" The phrase "molecules having sequence similarity to TGF ß" has been removed from claim 5. Thus, Applicants respectfully submit that claim 5 is in allowable form.

Rejections Under 35 U.S.C. §102(b)

Claims 1-4, 12, 13, 25, and 40 stand rejected under 35 U.S.C. §102(b) as being anticipated by Keifer (U.S. Pat. No. 5,620,867). The Examiner contends that Keifer discloses a BMP that contains the same sequence as BBP and thus anticipates the claimed SEQ ID No: 1 and inherently anticipates the claimed effects of BBP. The Examiner also argues that the claims do not require that "the claimed peptide increase the degree or rate of osteogenesis or calcification." However, as amended, claims 1, 3-4, 12, 13, 25, and 40 require that the claimed peptide increase the degree or rate of osteogenesis or calcification.

Applicants respectfully disagree with the Examiner's view of Keifer's teachings. For a prior art reference to anticipate the claimed invention, the prior art reference must contain every element of the claimed invention. *See Zenith Electronics v. PDI Communications Systems*, 522 F.3d 1348, 1363 (Fed. Cir. 2008). The protein that Keifer disclosed in Figures 3 and 5 is secreted phosphoprotein-24 (Spp-24). *See, e.g.*, Brochmann, E. J., *et al.*, *Bone morphogenetic protein-2 activity is regulated by secreted phosphoprotein-24 kd, an extracellular pseudoreceptor, the gene for which maps to a region of the human genome important for bone quality*, 58 Metabolism 644 (2009)("Brochmann 2009"). In contrast, the rejected claims are drawn to substantially pure BBP, a 2.1 kD peptide derived from the 24 kD phosphoprotein SPP-24. *See, e.g.,* Specification, ¶26. The claimed BBP and SPP-24 are not the same molecule. In fact, BBP is approximately 1/12th the size of the SPP-24 protein described in Keifer. Thus, Keifer does not disclose a substantially pure BBP.

Further, the claimed BBP peptide increases the rate or degree of osteogenesis or calcification, including in combination with BMP-2 and other BMPs. In contrast, there is no express or inherent evidence that SPP-24 increases the rate or degree of osteogenesis or calcification. Rather, studies have shown that the full length SPP-24 molecule, when combined with BMP, completely inhibits bone formation. *See* Brochmann, E.J., *et al.*, *Carboxy terminus of secreted phosphoprotein-24 kDa (spp24) is essential for full inhibition of BMP-2 activity*, 28 J. Orthopedic Research 1200 (2010)("Brochmann 2010"); Brochmann 2009, *supra*; Sintuu, C., *et al.*, *Full-length bovine spp24 [spp24(24-203)] inhibits BMP-2 induced bone formation*, 26 J. Orthopedic Res. 753 (2008)("Sintuu"). Brochmann 2009, Brochmann 2010, and Sintuu are enclosed with this Response. Thus, Keifer cannot anticipate

the claimed invention because Keifer does not disclose a substantially pure BBP, a 2.1 kD peptide that increases the rate or degree of osteogenesis or calcification.

The Examiner then argues that because the full-length SPP-24 protein disclosed in Keifer contains the BBP peptide, Keifer's disclosure inherently anticipates the claimed invention. The Examiner contends that "insofar as Keifer discloses a peptide comprising the amino acid sequence of SEQ ID NO: 1, then Keifer discloses....a peptide comprising any fragment of SEQ ID NO: 1, wherein the fragment increases the degree or rate of osteogenesis or calcification." However, "[u]nder the doctrine of inherency, if an element is not expressly disclosed in a prior art reference, the reference will still be deemed to anticipate...if the missing element is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill." *See Rosco, Inc. v. Mirror Lite Co.*, 304 F.3d 1373, 1380 (Fed. Cir. 2002). Further, [i]nherent anticipation requires that the missing descriptive material is necessarily present, not merely probably or possibly present, in the prior art." *Id.*

Here, Keifer does not disclose a substantially purified BBP which increases the degree or rate of osteogenesis or calcification, for example, by BMP-2. Instead, Keifer discloses the much larger SPP-24 protein, which when used in its entirety, inhibits osteogenesis by BMPs. *See, e.g.*, Brochmann 2010; Sintuu. Keifer does not in any way teach that a fragment of the SPP-24 protein disclosed increases the degree or rate of osteogenesis or calcification, including in combination with BMPs. Thus, one skilled in the art reading Keifer would not know that a particular fragment of the protein disclosed will increase the degree or rate of osteogenesis or calcification, for example, by BMPs. Thus, Applicants respectfully submit that Keifer does not expressly or inherently disclose all of the elements of the claimed invention, and therefore, Keifer cannot anticipate the claimed invention.

The Examiner further claims that to read Keifer as not disclosing a fragment of SPP-24 that increases the degree or rate of osteogenesis or calcification by BMP-2 is to argue that Applicants have themselves not enabled BBP. However, Applicants have enabled BBP, the claimed fragment of SPP-24 that increases the degree or rate of osteogenesis or calcification by BBP. Despite the fact that the full-length protein SPP-24 contains the sequence for BBP, SPP-24 and BBP are different proteins, and consequently do not necessarily have the same function. *See, e.g.*, Bohmann 2010; Sintuu. Further, in paragraph 26 of the specification,

Applicants acknowledge that "no function for SPP-24 has ever been published." Thus, Applicants have not attempted to enable SPP-24, as the invention is drawn to a peptide derived from SPP-24. Thus, Applicants respectfully submit that claims 1, 3-4, 12, 13, 25, and 40 are not expressly or inherently anticipated by Keifer.

Claims 1-4, 12, 13, 22, 25, and 38-40 also stand rejected under 35 U.S.C. §102(b) as being anticipated by Price (WO 96/21006). However, the Price reference has similar deficiencies as the Keifer reference. The Examiner contends that Price teaches the protein SPP-24 and that the amino acid sequence of SPP-24 includes the claimed SEQ ID NO: 1. The Examiner also contends that by disclosing the sequence for SPP-24, Price also inherently anticipates the claimed effect of the BBP peptide. Applicants respectfully disagree with the Examiner's interpretation of Price's teaching. Applicants respectfully contend that Price, like Keifer, teaches the use of the entire SPP-24 protein, not the BBP peptide portion of the protein. As discussed above, the full SPP-24 protein will act to completely inhibit BMP activity. *See* Brochmann, 2009, *supra*; Brochmann 2010, *supra*; Sintuu, *supra*. In contrast, the claimed peptide will increase the degree or rate of osteogenesis, for example, in combination with BMPs. Price does not expressly or inherently disclose the use of the specific 19 amino acid fragment comprising BBP that will function as claimed. As such, Price does not expressly or inherently anticipate the claimed peptide.

CONCLUSION

In view of the foregoing, Applicants respectfully submit that Claims 1, 3-5, 11-13, 22, 23, 25, and 38-43 are in allowable form, and the application is now in condition for allowance. Applicants request the Examiner to indicate all claims as allowable, and the pass the application to issue.

The Commissioner is authorized to charge any additional fees or credit any overpayments associated with this Amendment to Deposit Account 13-0206. Applicants further invite the Examiner to contact the undersigned representative at the telephone number below to discuss any matters pertaining to the present Application. The Examiner is requested to contact the undersigned if the Examiner has any questions concerning this Response, or if it will expedite the progress of this application.

Respectfully submitted,

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Date: June 16, 2011

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Enclosures:

Brochmann, E. J., *et al.*, *Bone morphogenetic protein-2 activity is regulated by secreted phosphoprotein-24 kd, an extracellular pseudoreceptor, the gene for which maps to a region of the human genome important for bone quality*, 58 Metabolism 644 (2009).

Brochmann, E.J., *et al.*, *Carboxy terminus of secreted phosphoprotein-24 kDa (spp24) is essential for full inhibition of BMP-2 activity*, 28 J. Orthopedic Research 1200 (2010).

Sintuu, C., *et al.*, *Full-length bovine spp24 [spp24(24-203)] inhibits BMP-2 induced bone formation*, 26 J. Orthopedic Res. 753 (2008).